

AMENDMENTS TO CLAIMS

1. (currently amended): A method for medium resolution typing of a target human leukocyte antigen (HLA) gene, which method comprises:

a) isolating a target leukocyte cell comprising a target HLA gene from a suitable sample and obtaining a preparation comprising a target HLA nucleotide sequence that is at least a part of said target HLA gene from said isolated target leukocyte cell and, optionally another nucleotide sequence not related to said target HLA gene;

b) providing a chip comprising a support suitable for use in nucleic acid hybridization having immobilized thereon an oligonucleotide probe complementary to said target HLA nucleotide sequence, said probe having 30 nucleotides or less and comprising a nucleotide sequence ~~that:~~

~~(i) — hybridizes under high stringency with a nucleotide sequence set forth in Table 1 or a complementary strand thereof, or~~

~~(ii) — has at least 90% identity to a nucleotide sequence set forth in Table 1~~ selected from the group consisting of SEQ ID NOS: 1-214 or a complementary strand thereof;
and at least one of each of the following oligonucleotide control probes: a positive control probe, a negative control probe, a hybridization control probe and an immobilization control probe; and

c) hybridizing said preparation obtained in step a) to said chip provided in step b) and assessing hybridization between said target HLA nucleotide sequence and/or said another nucleotide sequence and said probe comprised on said chip to determine the type of said target HLA gene.

2-3. (canceled)

4. (previously presented): The method of claim 1, wherein the suitable sample is selected from the group consisting of blood, saliva, hair, a human tissue that comprises a human nucleic acid, and any other human tissues containing nuclear cells.

5-6. (canceled)

7. (previously presented): The method of claim 1, wherein the target leukocyte cell is isolated from the suitable sample using a magnetic microbead.

8. (canceled)

9. (previously presented): The method of claim 1, wherein the preparation of the target HLA nucleotide sequence comprises a nucleic acid amplification step.

10-21 (canceled)

22. (previously presented): The method of claim 1, wherein the target HLA nucleotide sequence obtained in step a) is single-stranded DNA or RNA.

23. (canceled)

24. (previously presented): The method of claim 1, wherein a labeled target HLA nucleotide sequence is obtained in step a).

25. (canceled)

26. (original): The method of claim 1, wherein the another nucleotide sequence is complementary to the positive control probe, the negative control probe or the hybridization control probe comprised on the chip.

27. (canceled)

28. (original): The method of claim 1, wherein the probes comprised on the chip are modified.

29. (canceled)

30. (original): The method of claim 1, wherein the chip comprises 1-400 different types of probes.

31. (original): The method of claim 1, wherein the chip comprises multiple arrays of probes and each array comprises 1-400 different types of probes.

32-36. (canceled)

37. (previously presented): The method of claim 1, wherein multiple copies of a probe are immobilized on the chip.

38-40. (canceled)

41. (previously presented): The method of claim 1, wherein the positive control probe is complementary to a portion of the target HLA nucleotide sequence, a nucleotide sequence amplified synchronically with the target HLA nucleotide sequence or a synthetic nucleotide sequence.

42. (original): The method of claim 41, wherein the negative control probe has about 1-3 basepair mismatches when compared to the positive control probe.

43. (previously presented): The method of claim 1, wherein the hybridization control probe is complementary to a synthetic nucleotide sequence not related to the target HLA gene.

44-45. (canceled)

46. (original): The method of claim 1, wherein one end of the immobilization control probe is chemically modified and the other end of the immobilization control probe has a detectable label.

47-48. (canceled)

49. (original): The method of claim 1, wherein the hybridization reaction in step c) is conducted in a hybridization solution comprising sodium chloride/sodium citrate (SSC) and a surfactant.

50-52. (canceled)

53. (original): The method of claim 1, wherein the hybridization reaction in step c) is conducted at a temperature ranging from about 42°C to about 70°C.

54-56. (canceled)

57. (original): The method of claim 1, wherein the immobilization efficiency is assessed by analyzing a signal from the immobilization control probe.

58. (previously presented): The method of claim 1, wherein the overall hybridization efficiency is assessed by analyzing the hybridization between the hybridization control probe and a labeled synthetic nucleotide sequence not related to the target HLA gene.

59. (original): The method of claim 1, wherein the hybridization specificity is assessed by analyzing the ratio between the hybridization signal involving the positive control probe and the hybridization signal involving the negative control probe, and the ratio between the hybridization signal involving the positive hybridization control probe and the hybridization signal involving the negative hybridization control probe, and increased ratios indicating the increased hybridization specificity.

60. (previously presented): The method of claim 1, wherein, in hybridizations involving a group of closely related probes, a positive signal(s) is determined based on the following criteria:

- a) the ratio of the hybridization signal over background noise is more than 3;
- b) the ratio of the hybridization signal over a relevant positive control probe hybridization signal is within a predetermined range;

- c) comparing hybridization signals of all probes giving positive signals based on the steps of a) and b), or hybridization signals of two probes giving two strongest hybridization signals when only one probe giving positive signal based on the steps of a) and b), to determine whether the signal is positive or negative; and
- d) there are 2 or less than 2 positive signals involving the group of closely related probes.

61-77. (canceled)

78. (currently amended): The method of claim 1, wherein the chip comprises HLA probes comprising all nucleotide sequences set forth in Table 1 having SEQ ID NOS: 1-214 or complementary strands thereof.

79. (currently amended): The method of claim 1, wherein the chip comprises an HLA-A ~~nucleotide~~ probe, an HLA-B ~~nucleotide~~ probe, and an HLA-DRB1 ~~nucleotide~~ probe.

80. (previously presented): The method of claim 1, wherein multiple positive control probes are immobilized on the chip, and variations in length and sequence of the immobilized positive control probes, when hybridized with the target HLA nucleotide sequence or the another nucleotide sequence in the preparation provided in step a), create a group of hybridization signals having strong-to-weak or weak-to-strong orderly magnitude.

81. (new): The method of claim 1, wherein the chip comprises an HLA-A probe comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS: 1-94 or a complementary strand thereof.

82. (new): The method of claim 1, wherein the chip comprises HLA-A probes comprising all nucleotide sequences having SEQ ID NOS: 1-94 or complementary strands thereof.

83. (new): The method of claim 1, wherein the chip comprises an HLA-B probe comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS: 95-170 or a complementary strand thereof.

84. (new): The method of claim 1, wherein the chip comprises HLA-B probes comprising all nucleotide sequences having SEQ ID NOS: 95-170 or complementary strands thereof.

85. (new): The method of claim 1, wherein the chip comprises an HLA-DRB1 probe comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS: 171-214 or a complementary strand thereof.

86. (new): The method of claim 1, wherein the chip comprises HLA-DRB1 probes comprising all nucleotide sequences having SEQ ID NOS: 171-214 or complementary strands thereof.